REMARKS

Claims 23, 25, 45-48, 51 and 54-57 are pending in the subject application. Claim 54 is withdrawn from consideration by the Examiner as directed to a non-elected species. By this amendment, Claims 23, 46, and 51 have been amended. The amendments place the application in condition for allowance or in better form for appeal. Support for the amendments to Claims 23 and 46 can be found at least in the first paragraph of the Detailed Description of the Invention on page 10 of the application as filed. Support for the amendment to Claim 51 can be found at least in Claim 46. Entry of the amendments is respectfully requested.

Rejection under 35 U.S.C. §112, Second Paragraph

Dependent Claim 51 is rejected for reciting the term "mimetic" where there is insufficient antecedent basis for this term. Claim 51 has herein above been amended to delete "mimetic" and to clarify that it is the "agent" that comprises the specified amino acid sequence.

Rejections under 35 U.S.C. §103(a)

Claims 23, 25, 45-48, 51 and 55-57 are rejected as being unpatentable over Gaynor et al. (U.S. Patent No. 6,001,964) ("Gaynor") in view of DeGiorgio et al. (Nature Medicine 7(11): 1189-93, 2001) ("DeGiorgio").

Reconsideration and withdrawal of this rejection are respectfully requested.

Gaynor teaches peptides that bind to anti-ds-DNA antibodies that can be used to treat systemic lupus erythematosus. Gaynor does not teach treating cognitive dysfunction or lupus-induced cognitive dysfunction.

DeGiorgio teaches that "up to 80% of lupus patients experience CNS disease characterized by neuropsychiatric symptoms and cognitive decline" (page 1189, first paragraph). However, just because lupus patients can have cognitive decline does not render obvious from the prior art the presently claimed method of treating cognitive dysfunction in lupus patients. It is noted that SLE is marked by a wide variety of abnormalities including arthritis and arthralagias, nephritis, central nervous system manifestations, pleurisy, pericarditis, leukopenia or thrombocytopenia, hemolytic anemia, and the so-called "butterfly rash" (see, e.g., first two paragraphs of Column 1 of Gaynor). Gaynor indicates in paragraph one that "[o]ne of the most serious complications of SLE is lupus nephritis." DeGiorgio, in the Abstract, teaches that "[i]n systemic lupus erythematosus, antibodies against double-stranded DNA are a major contributor to renal disease." However, in contrast, DeGiorgio teaches that "[t]he mechanism of CNS injury that accounts for these cognitive and psychological impairments is unknown" (see end of first paragraph of DeGiorgio on page 1189). Further, in the Discussion, DeGiorgio states that "the pathogenesis of CNS disease in lupus has remained elusive" (first paragraph on page 1191).

The present invention satisfies the well-recognized need for determining the cause of cognitive dysfunction in SLE and developing a treatment based on that cause. As set forth in the subject application in the beginning of the Detailed Description of the Invention on page 10 of the application as filed:

> "The present invention is based on the discovery that a cause for cognitive dysfunction in SLE is the entry across the blood-brain barrier of anti-dsDNA antibodies that bind to the NR2 subunit of neuronal NMDA receptors, and the subsequent apoptosis of those neurons in the brain, particularly the hippocampus. Experiments establishing this discovery are provided in Example 1 and further confirmed in Example 2."

The Summary of Example 1 on pages 15-16 provides:

> "Patients with systemic lupus erythematosus (SLE) may experience progressive cognitive disabilities. We previously demonstrated that SLE patients produce anti-DNA antibodies that cross-react with the NR2a and 2b subunits of the NMDA receptors, and that these antibodies can mediate excitotoxic death of neurons. We now demonstrate that mice producing anti-NR2 antibodies have no neuronal damage until there is a breakdown of the blood-brain barrier. Once the antibodies gain access to the brain, they bind preferentially to hippocampal neurons, and cause neuronal death with resulting cognitive dysfunction and associated abnormalities in magnetic resonance spectroscopy. This study provides a model for systemic immune responses in SLE leading to cognitive impairment."

As explained in the Discussion on page 18,

> "These data provide a model for cognitive decline in SLE. The model requires the presence of anti-NR2 antibodies found in approximately 25 to 50 percent of patients with SLE (Sharma et al., 2003), but also requires a breakdown in the blood-brain barrier. This breakdown might occur as a consequence of disease activity, such as cerebral vasculitis, but might also occur as a consequence of infection or stress and catecholaminergic excess, two conditions known to abrogate the integrity of the blood-brain barrier (Xaio et al, 2001; Abdel-Rahman et al., 2002; Esposito et al., 2002; Friedman et al., 1996). Thus, there is an explanation for the observation that cognitive decline does not parallel disease activity."

Accordingly, applicants respectfully maintain that the cited references do not render obvious the presently claimed invention. Reconsideration and withdrawal of this rejection are respectfully requested.

Request for re-instatement of withdrawn species claim

Re-instatement and consideration of withdrawn dependent species Claim 54 are respectfully requested (37 CFR §1.141, MPEP §806.04(d)).

CONCLUSIONS

In view of the amendments and remarks made hereinabove, reconsideration and withdrawal of the rejections set forth in the June 22, 2010 Office Action and passage of the pending claims to allowance are respectfully requested. If there is any minor matter preventing the allowance of the subject application, the Examiner is requested to telephone the undersigned attorney.

No fee is deemed necessary in connection with this reply. However, if any fee is required to maintain the pendency of the subject application, authorization is hereby given to withdraw the amount of any such fee from Deposit Account No. 01-1785.

Respectfully submitted,

AMSTER, ROTHSTEIN & EBENSTEIN LLP
Attorneys for Applicants
90 Park Avenue
New York, NY 10016
(212) 336-8000

Dated: August 20, 2010
New York, New York

By /Alan D. Miller/
Alan D. Miller, Reg. No. 42,889